REMARKS

Claims 1, 3, 5-49 are pending. Claims 3, 7, 8, and 20-47 are withdrawn from consideration. Claims 1, 2, 4-6, and 9-19 are currently being examined. Claim 1 has been amended; claims 2 and 4 have been cancelled without prejudice; and new claims 48 and 49 have been added. No new matter has been added by virtue of these amendments and additions. The claim amendments and additions are supported by the specification and the originally-filed claims.

In particular, support for the amendment to claim 1 can be found in the specification, for example, on page 38 and Figure 3. Support for new claims 48 and 49 can be found in the specification, for example, on page 9.

Amendment and cancellation should in no way be construed as an acquiescence to any of the Examiner's rejections. The amendments to, or cancellation of, the claims are being made solely to expedite prosecution of the present application and do not, and are not intended to, narrow the claims in any way. Applicants reserve the option to further prosecute the same or similar claims in the instant or in a subsequent patent application.

Election/Restrictions

Applicant would like to thank the Examiner for granting the request to examine Groups I and II together. However, contrary to the assertion at page 2 of the Office Action, Applicants did not assert that the inventions of Groups I and II are indistinct. Rather, Applicants merely stated that Groups I and II were related and thus simultaneous examination of the groups together would not place an undue burden on the Examiner.

Furthermore, Applicants respectfully request that claim 3 be reinstated or that an explanation be provided for why it was withdrawn from consideration. As stated in the Response to Restriction Requirement dated January 6, 2003, Applicants elected psoralen as a species of ***crosslinking*** moiety as referenced in claims 1 and 5. As distinct from the crosslinking moiety, claims 2 and 3 refer to a ***linking*** moiety which connects parts of the conjugate (e.g., a target moiety and a pairing oligonucleotide) in certain embodiments of the claims. Accordingly, claims 2 and 3 read on the elected species of psoralen as the crosslinking moiety.

Objections to the Specification

The disclosure was objected to as containing informalities because U.S. applications were cited without reference to their current status. As requested, appropriate correction has been made. Additionally, the specification was objected to for containing minor errors of a typographical nature. As requested, Applicants have corrected all discernable typographical errors. Accordingly, withdrawal of the objections to the specification is respectfully requested.

Rejection of Claims 1, 2, 4-6 and 9-19 under 35 U.S.C. § 103(a)

Claims 1, 2, 4-6 and 9-19 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Horn et al (US 6,465,175) or Guire et al (US 6,514,768) in view of Kuimelis et al (WO 99/51773). The rejection is respectfully traversed.

Horn et al. is relied on for disclosing single stranded polynucleotide capture extender molecules that hybridize to a support bound probe. The Office Action states that:

> Horn et al discloses . . . a support bound probe "***capture extenders***," [that] hybridize to the analyte polynucleotide and to capture probes, which are in turn covalently bound to a solid support. Thus, capture extender molecules are ***single-stranded polynucleotide chains*** having a first polynucleotide sequence region containing a nucleic acid sequence C-1 which is complementary to a sequence of the analyte, and a second, noncomplementary region having a capture probe recognition sequence C-2.*** (Office Action at 4, emphasis added)

Horn is further relied on for teaching the following:

> ***[T]he total number of oligonucleotide segments in the ***multimer*** will usually be in the range of about 3 to 1000, more typically in the range of about 10 to 100[.] [T]he oligonuleotide segments of the multimer may be covalently linked directly to each other through phosphodiester bonds or through other cross-linking agents that are capable of cross-linking nucleic acid or modified nucleic acid strands. Horn discloses a linker moiety as ethylene glycol .... (Office Action at 5, emphasis added)

Horn et al. teaches that the ***capture extender*** molecules are single stranded polynucleotide chains. Notably, and in contrast to the currently claimed embodiment, Horn et al. fails to teach or suggest that such ***capture extender*** molecules may contain a linking moiety that

covalently attaches a target moiety to a pairing oligonucleotide wherein the linking moiety terminates extension by a polymerase. The Action relies on Horn for teaching a linking moiety; however, the linking moiety is disclosed in association with a ***nucleic acid multimer*** and not in association with the ***capture extender*** molecule. The nucleic acid multimer and capture extender molecules appear to be completely separate elements of Horn et al. as illustrated by the fact that such terms are separately defined in the specification. The nucleic acid multimer is described by Horn et al. as follows:

> The terms "nucleic acid multimer" or "amplification multimer" are used herein to refer to a linear or branched polymer of the same repeating single-stranded polynucleotide segments, each of which contains a region where a labeled probe can hybridize, i.e., contains a nucleic acid sequence complementary to a nucleic acid sequence contained within a labeled probe; the oligonucleotide segments may be composed of RNA, DNA, modified nucleotides or combinations thereof.*** (Horn et al. at column 7, lines 1-10)

Since the nucleic acid multimer and the capture extender molecules are distinct components of the Horn et al. system, the teaching of a linking moiety in association with the nucleic acid multimer fails to teach or suggest the currently claimed embodiments of the instant invention.

Further, the Action states that Horn et al. discloses a linker moiety that is ethylene glycol at col. 11, line 42. Applicants wish to note that such linker moiety is disclosed as a means to attach a label (e.g., a dye molecule) to an oligonucleotide probe to create an oligomer-label conjugate (see e.g., column 10, lines 11 to column 11, line 61). Therefore, the use of ethylene glycol as a linking moiety is disclosed in association with yet another element of the Horn et al. system, namely a labeled oligonucleotide probe, and is not taught in association with either the nucleic acid multimer nor the capture extender molecules. Accordingly, Horn et al. fails to teach or suggest the currently claimed embodiment which is directed, at least in part, to a conjugate comprising a target moiety and a pairing oligonucleotide which are covalently linked by a linking moiety.

Kuimelis et al. fails to cure the deficiencies of Horn et al. In particular, Kuimelis et al. is relied on for teaching that psoralen may be used to covalently cross-link a nucleic acid-protein conjugate to a capture probe. However, Kuimelis et al., like Horn et al., fails to teach a linking moiety that covalently attaches a target moiety to a pairing oligonucleotide wherein the linking moiety terminates extension by a polymerase.

Accordingly, the cited references, either alone or in combination, fail to teach or suggest the currently claimed embodiments. Reconsideration and withdrawal of the rejection is respectfully requested.

Guire et al. is relied upon for disclosing a system that includes a multiligand conjugate containing a plurality of active domains. The Office Action states:

> ***The individual ligands can be attached to a core atom or molecule in any suitable manner and/or order, e.g., individually or together (e.g. in linear sequence and at a single location or at a plurality of locations). The ligands are attached to the core simultaneously, e.g., under similar reaction conditions. Optionally, the ligand serving as the third ligand is attached to the core after hybridization between the address oligonucleotide of the master array and the complementary oligonucleotide provided by the multi-ligand conjugate. (Office Action at 5-6)

The Examiner notes that Guire et al. fails to teach a cross-linking moiety. The Action relies on Kuimelis et al. for teaching that psoralen may be used to covalently attach a nucleic acid-protein fusion to a capture probe via cross-linking. The Action states that:

> It would have been obvious to use psoralen as the cross linking moiety in the solid bound probe of . . . Guire (array probe) as taught by Kuimelis. ... It is well known in the art that cross-linking results in a stable component of the probe. One would be motivated to produce a stable cross linked probe since specific hybridization of the probe with a target leads to pharmaceutical drugs with binding specificity and in vivo stability. (Office Action at 7)

Contrary to the assertions in the Office Action, it would not have been obvious to combine the teachings of Guire et al. with the teachings of Kuimelis et al. In fact, Guire et al. teaches away from any combination with the relied upon disclosure of Kuimelis et al. and from the currently claimed embodiment which is directed, at least in part, to a support bound probe that comprises a capture oligonucleotide and a conjugate that is ***covalently attached*** to either the capture oligonucleotide or the solid support.

In particular, Guire et al. is directed to a replicable probe array and a system for producing substantially identical assay arrays from a master array (see e.g., abstract, Figure 1A, and the description of Figure 1A at column 4, lines 28-51). Guire et al. discloses a master array which is an array of nucleic acid sequences (referred to as address ligands) attached to a solid support. Nucleic acid sequences called multi-ligand conjugates are then hybridized to the master

array. The multi-ligand conjugates contain a sequence that hybridizes to the address ligands, a sequence that binds to a target nucleic acid, and a binding ligand that will attach the multi-ligand conjugate to a solid support to form the assay array. This is a ***transitory structure*** formed in the process of making an assay array (see e.g., column 4, lines 40-42). The multi-ligand conjugates are then ***dissociated*** from the address ligands thereby forming the assay array and recovering the master array (see e.g., Figures 1A and 1B and the description at column 4, lines 47-51). Using such a system, multiple assay arrays that are essentially identical may easily be formed from a single reusable master array.

Key to the system described in Guire et al. is the dissociation of the multi-ligand conjugate from the address ligands of the master arrays. This allows formation of new assay arrays and recovery of the reusable master array. If the multi-ligand conjugates were to be covalently attached to the master array (e.g., using a cross-linker such as psoralen), it would destroy the functionality of the Guire et al. system and result in a single, non-replicable, non-reusable assay array. Accordingly, there would be no motivation to combine the teachings of Kuimelis et al. with the teachings of Guire et al. Furthermore, Guire et al. appears to teach away from the currently claimed embodiments which are directed, at least in part, to a ***support bound probe*** that comprises a capture oligonucleotide and a conjugate that is ***covalently attached*** to either the capture oligonucleotide or the solid support.

Accordingly, the cited references, either alone or in combination, fail to teach or suggest the currently claimed embodiments. Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

Applicants consider the Response herein to be fully responsive to the referenced Office Action. Based on the above Remarks and Amendment, it is respectfully submitted that this application is in condition for allowance. Accordingly, allowance of the pending claims is requested. If a telephone conversation with Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 832-1000.

Respectfully submitted,

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Dated: June 13, 2003

Customer No. 25181